

PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT
(PCT Article 36 and Rule 70)

REC'D 20 JAN 2005

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Applicant's or agent's file reference RE/PG5044	FOR FURTHER ACTION See Notification of Transmittal of International Preliminary Examination Report (Form PCT/PEA/416)	
International application No. PCT/EP 03/13803	International filing date (day/month/year) 04.12.2003	Priority date (day/month/year) 06.12.2002
International Patent Classification (IPC) or both national classification and IPC C07H21/00		
Applicant GLAXO GROUP LIMITED et al.		

<p>1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.</p> <p>2. This REPORT consists of a total of 5 sheets, including this cover sheet.</p> <p><input type="checkbox"/> This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).</p> <p>These annexes consist of a total of sheets.</p>
<p>3. This report contains indications relating to the following items:</p> <ul style="list-style-type: none"> I <input checked="" type="checkbox"/> Basis of the opinion II <input type="checkbox"/> Priority III <input type="checkbox"/> Non-establishment of opinion with regard to novelty, inventive step and industrial applicability IV <input type="checkbox"/> Lack of unity of invention V <input checked="" type="checkbox"/> Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement VI <input type="checkbox"/> Certain documents cited VII <input type="checkbox"/> Certain defects in the international application VIII <input type="checkbox"/> Certain observations on the international application

Date of submission of the demand 09.06.2004	Date of completion of this report 20.01.2005
Name and mailing address of the International Preliminary examining authority:  European Patent Office - P.B. 5818 Patentlaan 2 NL-2280 HV Rijswijk - Pays Bas Tel. +31 70 340 - 2040 Tx: 31 651 epo nl Fax: +31 70 340 - 3016	Authorized Officer Macchia, G Telephone No. +31 70 340-4078



INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/EP 03/13803

I. Basis of the report

1. With regard to the **elements** of the international application (*Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17)*):

Description, Pages

1-29 as originally filed

Sequence listings part of the description, Pages

1-7 received on 18.05.2004 with letter of 17.05.2004

Claims, Numbers

1-5 as originally filed

Drawings, Sheets

1/4-4/4 as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language: , which is:

- the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
- the language of publication of the international application (under Rule 48.3(b)).
- the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- contained in the international application in written form.
- filed together with the international application in computer readable form.
- furnished subsequently to this Authority in written form.
- furnished subsequently to this Authority in computer readable form.
- The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

- the description, pages:
- the claims, Nos.:
- the drawings, sheets:

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5. This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)).

(Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	1-5
	No:	Claims	
Inventive step (IS)	Yes:	Claims	1-5
	No:	Claims	
Industrial applicability (IA)	Yes:	Claims	1-5
	No:	Claims	

2. Citations and explanations

see separate sheet

**INTERNATIONAL PRELIMINARY
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Reference is made to the following documents:

D1: WO 02/102825 A (CATCHPOLE IAN RICHARD; GLAXO GROUP LTD (GB)) 27 December 2002.

D2: Weeratna R.D. et al.: " CpG DNA induces stronger immune responses with less toxicity than other adjuvants " Vaccine, 2000, vol. 18, pages 1755-1762.

The document D2 was not cited in the international search report.

Re Item V

Reasoned statement with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

- 1). Present claims 1-5 meet the requirements of Article 33(2) PCT because their subject-matter was not disclosed in the available prior art (see however possible later relevance of document D1, published before the filing date of present application but after the priority date of present application).

- 2). The document D2 is regarded as being the closest prior art and shows a phosphorothioate oligonucleotide GpG ODN 1826 having the sequence: **tccatgacgttcctgacgtt** (D2: see relevant passages throughout the entire document).

The subject-matter of claim 1 differs from the disclosure of D2 in that an oligonucleotide having the same sequence as D2, attached to a certain LNA sequence is concerned.

The subject-matter of claim 2 differs from the disclosure of D2 in that oligonucleotides as from SEQ ID NO:3, 14, 18 or 20 are concerned.

The subject-matter of claim 3 differs from the disclosure of D2 in that a complex related to the oligonucleotides of claims 1 and 2 is concerned.

The subject-matter of claims 4 and 5 differs from the disclosure of D2 in that a method for manufacturing a LNA-CpG conjugate is concerned.

The problem to be solved by the present invention may therefore be regarded as

the provision of further CpG oligonucleotides and of methods related thereto.

The solution to this problem is considered as involving an inventive step (Article 33(3) PCT) because document D2 provides, neither alone nor in combination with any other document, no suggestion that could be considered by the skilled man as an incentive to obtain CpG-LNA conjugates.

Consequently, the skilled person should have made use of inventive skills in order to arrive at the subject-matter claimed.

- 3). The industrial applicability of the subject-matter of claims 1-5 is acknowledged (Article 33(4) PCT).

In addition to the previous objections, the following should be remarked:

- 4). Claim 2 should not depend on claim 1 because SEQ ID NO:14 and 20 do not contain both the sequences indicated in claim 1 (Article 6 PCT).
- 5). SEQ ID NO:3 provided by the Applicant in the Sequence listing does not correspond to SEQ ID NO:3 of page 3. Indeed SEQ ID NO:3 on page 3 contains an optional residue (X) between the two halves of the oligonucleotide, which is missing in SEQ ID NO:3 as provided later by the Applicant.

The oligo 4 of page 5 (CpG 2006) has no sequence in the sequence listing. Indeed, the reference to SEQ ID NO:1 is wrong and SEQ ID NO:1, as provided later by the Applicant refers to the oligonucleotide as shown in page 3 of present application.

SEQ ID NO:12 provided later by the Applicant in the sequence listing does not correspond to SEQ ID NO:12 on page 16.

In the table on page 19, the SEQ ID NO of oligonucleotide PTOCpG2 is probably mistyped and it should be SEQ ID NO:18 instead that SEQ ID NO:1.